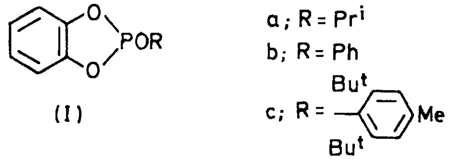
Mechanisms of Antioxidant Action: Antioxidant Activity of Products Derived from *o*-Phenylene Phosphites

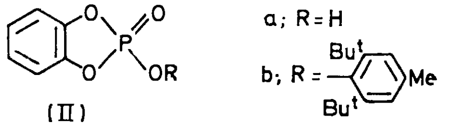
By **Kenneth J. Humphris** and **Gerald Scott,*** Department of Chemistry, The University of Aston in Birmingham, Gosta Green, Birmingham B4 7ET

Products known to be formed in the reaction between 4-methyl-2,6-di-t-butylphenyl *o*-phenylene phosphite (Ic) and cumene hydroperoxide, namely the corresponding phosphate (IIb) and its transformation products (IIa) and (III), are powerful antioxidants in autoxidations catalysed by hydroperoxides and are effective catalysts for the decomposition of cumene hydroperoxide in which they function primarily as Lewis acids. Only (IIa) and (III) satisfy the requirements of the Lewis acid species and although positive identification has not been made a mechanism is proposed involving these species which accounts for the experimental facts.

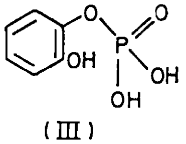
It has been shown[1-3] that the antioxidant activity of *o*-phenylene phosphites (catechol phosphites) (I) is not due to the phosphites themselves but to a catalytic species derived from them. A number of phosphorus-containing species formed in the reaction of (Ic) with cumene hydroperoxide have been identified and synthesised.[2] These include the cyclic phosphates (II) and the hydrolysis product (III) from (IIa). The present study is concerned with the measurement of the antioxidant and peroxidase activity of these products in an attempt to identify the catalytic species.



(I)



(II)



(III)

RESULTS AND DISCUSSION

The catechol phosphate (IIb) was found to behave very similarly to the corresponding phosphite (Ic)[4] in the azobisisobutyronitrile (AZBN)-initiated autoxidation of cumene. Like the phosphite it is not initially an antioxidant but it becomes an effective inhibitor after a period of oxidation (Figure 1). No pro-oxidant stage was evident. Very similar results were obtained with 2-hydroxy-2-oxo-1,3,2-benzodioxaphosphole (IIa) and its hydrolysis product (III) except that complete inhibition was achieved in a much shorter time (*ca.* 10%) and with a much smaller absorption of oxygen (*ca.* 20%).

With cumene hydroperoxide as initiator, autoretardation was again observed with the catechol phosphate (IIb) but in contrast to the parent phosphite (Ic) under the same conditions[4] it showed neither a pro-oxidant effect nor gas evolution (Figure 2) nor did it achieve complete inhibition as rapidly at the same molar concentration. The catechol phosphate (IIa) on the other hand shows very similar gas evolution (see Figure 3) to the catechol hindered-phenyl phosphite (Ic).[4] In contrast to the latter, there was no apparent absorption of oxygen and the gas was evolved in *ca.* 1/10 the time. However, the curves are not coincident in the presence of and absence of oxygen and oxidation by oxygen may be involved.

It was reported earlier[1] that triphenyl phosphate was inert toward hydroperoxide. The catechol phosphate (IIb) on the other hand is an effective catalyst for the decomposition of cumene hydroperoxide and it can be seen from Figure 4 that at the same concentration it gives the same rate of decomposition in the pseudo-first-order

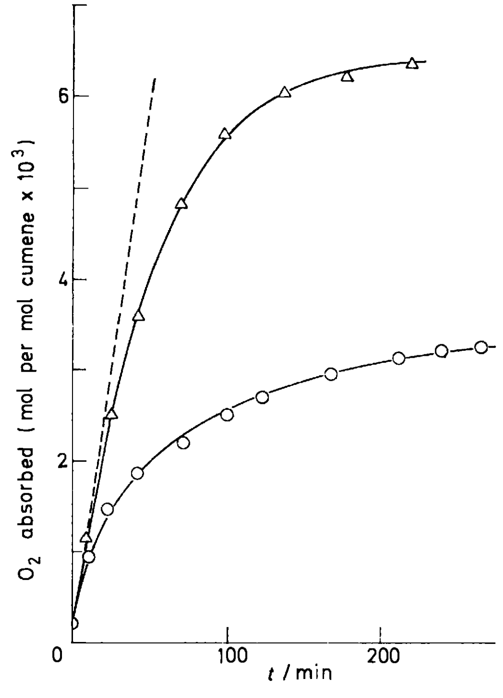


FIGURE 1 Inhibition of the oxidation of cumene in oxygen by catechol phosphate (IIb) at 75° C: — — — without antioxidant: △ with 0·005M-phosphate; ○ with 0·02M phosphate. $[AZBN]_0$ = 0·02M

---

[1] (*a*) K. J. Humphris and G. Scott, *Pure Appl. Chem.*, 1973, **36**, 163; (*b*) *J.C.S. Perkin II*, 1973, 826.

[2] K. J. Humphris and G. Scott, *J.C.S. Perkin II*, 1973, 831.

[3] K. J. Humphris and G. Scott, unpublished work.

[4] G. Scott, *Pure Appl. Chem.*, 1972, **30** (No. 1—2), 267.

stage as does the phosphite (Ic). The Arrhenius plot for the catalytic process was identical with that reported earlier for the corresponding phosphite[1] ($E_a = 60{\cdot}9$ kJ mol^{-1}). Unlike the latter, however, which shows an initial fast rate of oxidation before the catalytic stage, the phosphate gives an auto-accelerating rate before this stage is reached. It was found that during the auto-accelerating stage of the peroxide decomposition no radicals were produced as evidenced by the fact that the addition of the phosphate to cumene hydroperoxide (CHP)-initiated polymerisation did not accelerate the rate of polymerisation of styrene.[3] The evidence, taken together, suggests that the hindered-phenyl phosphate is not involved as a major intermediate in the reaction sequence which leads to the catalytic species.

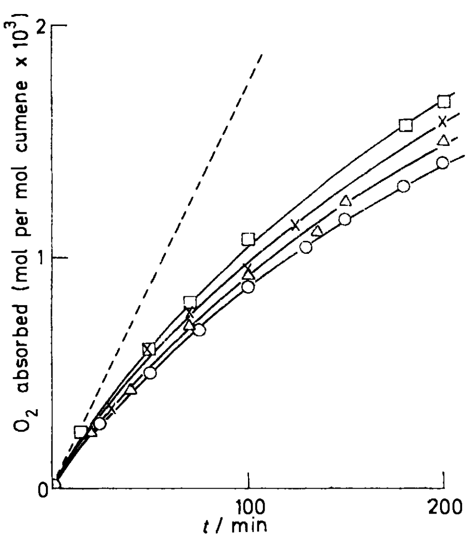


FIGURE 2 Inhibition of the oxidation of cumene in oxygen by catechol phosphate (IIb) at 75°: — — — without antioxidant; ○ 0·005M-phosphate; △ 0·01M-phosphate, × 0·02M-phosphate; □ 0·03M-phosphate. $[\mathrm{CHP}]_0 = 0{\cdot}2$M (all curves are the average of four runs)

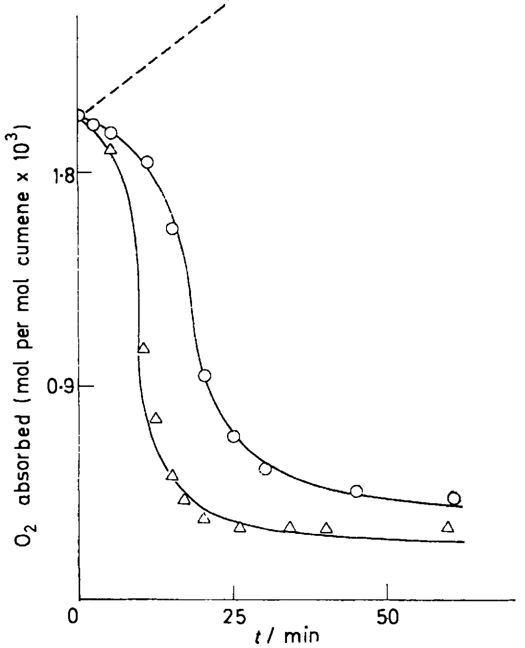


FIGURE 3 Gas evolution during the reaction of 0·02M-catechol phosphate (IIa) with 0·2M-cumene hydroperoxide in cumene at 75°: — — — without phosphate in oxygen; ○ with phosphate in oxygen; △ with phosphate in nitrogen

The products (IIa) and (III) were very sparingly soluble in chlorobenzene. Nevertheless they were both found to be very powerful catalysts for the decomposition of cumene hydroperoxide giving pseudo-first-order kinetics with no apparent preliminary reaction. Comparative first-order rate constants for the four phosphorus-containing species are listed in the Table. The values for (IIa) and (III) must be considered to be minimum values in view of the heterogeneity of the reaction.

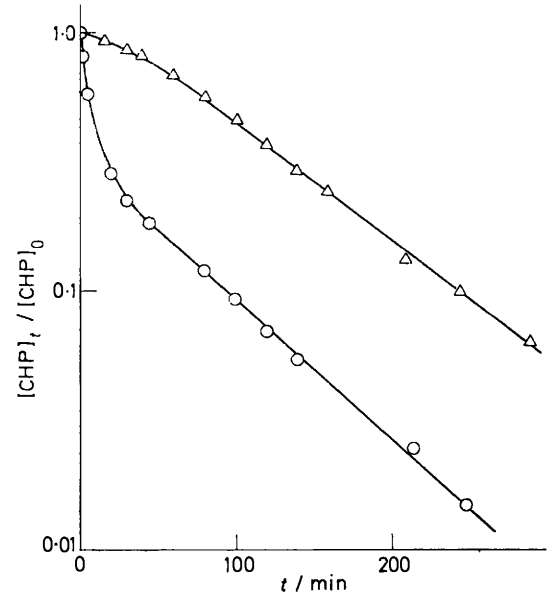


FIGURE 4 First-order plot for the decomposition of 0·2M-cumene hydroperoxide in chlorobenzene at 75°: ○ 0·04M-catechol phosphite (Ic); △ 0·04M catechol phosphate (IIb)

Pseudo-first-order rate constants for the decomposition of cumene hydroperoxide in the presence of phosphorus-containing species (P) in chlorobenzene at 75°: $[\mathrm{CHP}]_0 = 0{\cdot}2$M, $[\mathrm{P}]_0 = 0{\cdot}02$M

P	10^4k_1/s^{-1}
(Ic)	1·1
(IIb)	1·2
(IIa)	84
(III)	2·5

The products obtained by the reaction of the catechol phosphate (IIb) with hydroperoxide vary much less with the ratio of hydroperoxide to the phosphorus compound (Figure 5) than in the case of the corresponding phosphite.[2]

The yield of α-methylstyrene is interesting because it tends toward the same limiting value as it does in the phosphite catalysed reaction.[2] On the basis of an initial stoicheiometric reaction to give α-cumyl alcohol (and hence α-methylstyrene) followed by an entirely

Lewis acid catalysed process to give phenol and acetone, the yield of α-methylstyrene should fall asymptotically to zero. This is certainly not the case in chlorobenzene although it was observed earlier that this situation is approached in nitrobenzene.[2] It must be concluded from this that the ratio of products formed in the catalytic stage of the reaction is solvent dependent and that in non-polar solvents radical-generating processes must be involved at all stages. This accords with the results reported earlier for the polymerisation of styrene[1a] from which it was seen that for two catechol phosphite esters in the presence of a constant concentration of hydroperoxide the maximum rate of polymerisation was achieved at a $[\mathrm{CHP}]_0 : [\mathrm{Phosphite}]_0$ ratio of *ca.* 13.

An interesting fact emerging from Figure 5 is that the catalytic species plays a dominant role in the reaction of the catechol phosphate (IIb) with cumene hydroperoxide at all ratios whereas in the case of the corresponding phosphite, this occurs only after the destruction of 1 mol. equiv. of hydroperoxide.[2]

Of the compounds identified, only the acidic species (IIa) and (III) satisfy the requirements of the unknown Lewis acid. A mechanism which accounts for the extremely powerful catalytic activity of (IIa) toward cumene hydroperoxide is given in Scheme 1.

The postulated intermediates bear a strong resemblance to those involved in the hydrolysis of the nucleic acids[5] and high catalytic activity in hydrogen and hydroxide ion transfer appears to be a general characteristic of cyclic phosphates. It has been pointed out by Brown and Higson[6] that the abnormal ease of hydrolysis of the diesters of phosphoric acids derived from 1,2-diols is due to the participation of the vicinal hydroxy-group during the reaction. In the ionised form (V), the charge can be shared between the oxygen of the phosphorus (Va) and the oxygen of the catechol (Vb). In the presence of water the catechol cyclic phosphate hydrolyses extremely rapidly even in neutral solution (Scheme 2).[2]

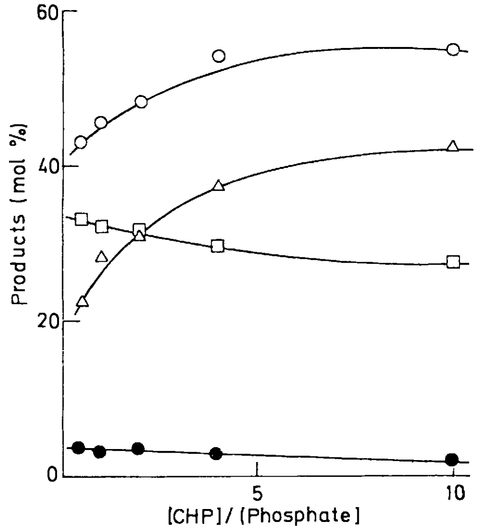
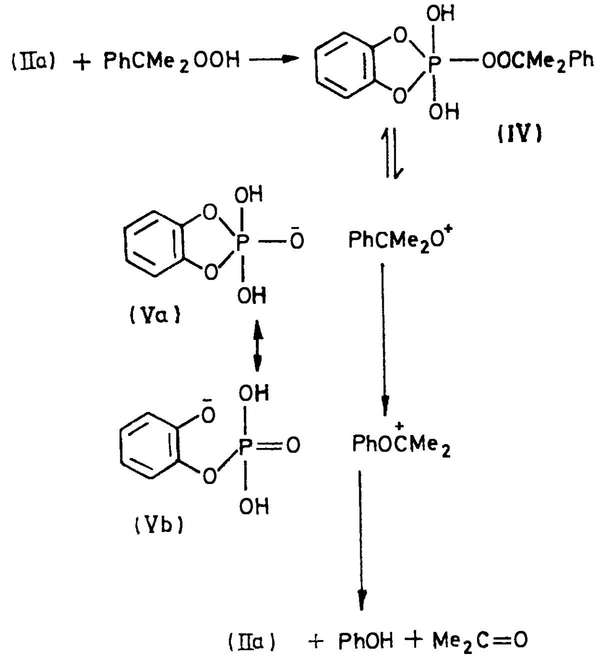
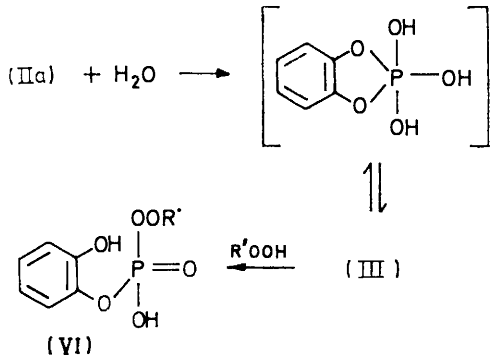


FIGURE 5 Products formed from the reaction of cumene hydroperoxide with catechol phosphate (IIb) in chlorobenzene at 75° at varying ratios of hydroperoxide to catalyst: ○ phenol; △ acetone; □ α-methylstyrene; ● acetophenone



SCHEME 1



SCHEME 2

The acyclic compound (III) is not such an active catalyst for peroxide decomposition since in this case a hydroxy-group has to be displaced and the sequence of reactions involved is energetically less favourable due to the absence of the anion.

In the case of the sterically hindered phenyl ester, the rate of initial attack of hydroperoxide is slower but leads ultimately to the same catalytic species (VI) in the presence of by-product water, together with the observed 4-methyl 2,6-di-t-butylphenol (Scheme 3).

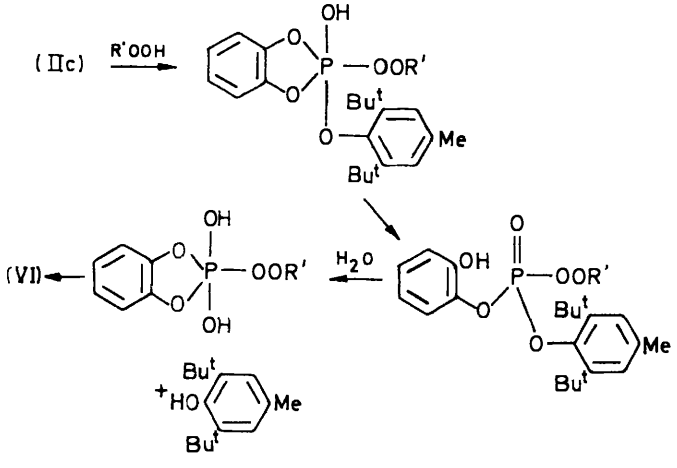
The formation of free radicals can be explained on the basis of an alternative dissociation of the peroxide (IV) which is favoured in non-polar solvents. Compounds of this type have been shown previously to be very unstable[7] and in the present case electron delocalisation will also favour dissociation (Scheme 4).

[5] D. M. Brown and A. R. Todd, *Ann. Rev. Biochem.*, 1955, **34**, 311.

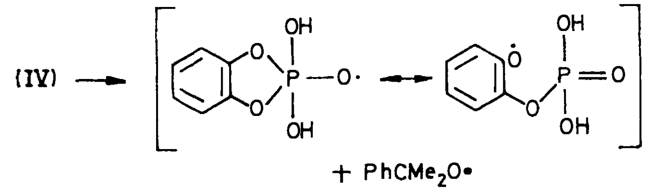
[6] D. M. Brown and H. M. Higson, *J. Chem. Soc.*, 1957, 2034.

[7] G. Sornovski and J. H. Brown, *Chem. Rev.*, 1966, **66**, 529.

Tertiary alkoxyl radicals are known to induce a chain decomposition of hydroperoxides[8] to give alcohol and oxygen as major products and ketones and methane as minor products (Scheme 5).



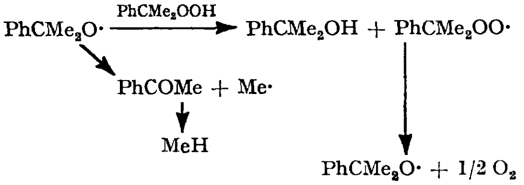
SCHEME 3



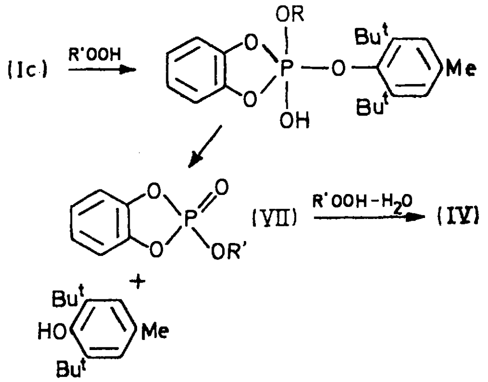
SCHEME 4

All these products (or their further transformation products) were identified.[2]

It seems likely that the active catalytic species (IV) may be formed directly from the cyclic phosphate (Ic). Removal of the hindered phenyl group by elimination of the corresponding phenol gives rise to an alkyl phosphate (VII) which by analogy with the analogous phosphites would be expected to react much more rapidly than (IIb) with hydroperoxide.[1]



SCHEME 5



SCHEME 6

The powerful antioxidant behaviour of the cyclic phosphates in polyethylene has been described elsewhere.[9]

EXPERIMENTAL

The oxygen absorption procedure, the methods of product analysis and the synthesis of reagents have all been described in previous publications.[1-4,10]

We thank Monsanto Chemicals, U.K., for a research grant to K. J. H.

[3/1065 *Received, 24th May*, 1973]

---

[8] E. R. Bell, J. H. Raley, F. F. Rust, F. H. Seubold, and W. E. Vaughan, *Discuss. Faraday Soc.*, 1951, **10**, 242.

[9] G. V. Hutson and G. Scott, *J. Polymer Sci., Part C*, 1973, **40**, 67.

[10] B. W. Evans and G. Scott, *European Polymer J.*, in the press.